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10/533799

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JC17 Rec'd PCT/PTO 0.4 MAY 2005

In the Claims

Please amend the claims according to the claim listing provided below.

1. (currently amended) A compound of Formula (I):

$$\begin{array}{c|c}
 & R_2 & O \\
 & R_1 & R_4 \\
\hline
 & (I)
\end{array}$$

wherein:

R₁ is C₁₋₈ alkyl, C₃₋₆ cycloalkyl or C₁₋₆ haloalkyl, wherein the C₁₋₈ alkyl, C₃₋₆ cycloalkyl and C₁₋₆ haloalkyl groups are optionally substituted with 1, 2, 3 or 4 substituents selected from the group consisting of C₁₋₆ acyl, C₁₋₆ acyloxy, C₂₋₆ alkenyl, C₁₋₆ alkoxy, C₁₋₆ alkyl, C₁₋₆ alkylcarboxamido, C₂₋₆ alkynyl, C₁₋₆ alkylsulfinyl, C₁₋₆ alkylsulfonyl, C₁₋₆ alkylthio, C₁₋₆ alkylureyl, amino, C₁₋₆ alkylamino, aryl, substituted aryl, C₁₋₆ dialkylamino, carbo C₁₋₆ alkoxy, carboxy, cyano, C₃₋₆ cycloalkyl, C₁₋₆ dialkylcarboxamido, halogen, C₁₋₆ haloalkoxy, C₁₋₆ haloalkylsulfinyl, C₁₋₆ haloalkylsulfinyl, C₁₋₆ haloalkylsulfinyl, C₁₋₆ haloalkylsulfinyl, heterocyclyl, hydroxyl, nitro and thiol;

R₂, R₃ and R₄ are each independently selected from the group consisting of H, C₁₋₆ acyl, C₁₋₆ acyloxy, C₂₋₆ alkenyl, C₁₋₆ alkoxy, C₁₋₆ alkyl, C₁₋₆ alkylcarboxamido, C₂₋₆ alkynyl, C₁₋₆ alkylsulfinyl, C₁₋₆ alkylsulfonyl, C₁₋₆ alkylthio, C₁₋₆ alkylureyl, amino, C₁₋₆ alkylamino, C₁₋₆ dialkylamino, carbo C₁₋₆ alkoxy, carboxy, cyano, C₃₋₆ cycloalkyl, C₁₋₆ dialkylcarboxamido, halogen, C₁₋₆ haloalkoxy, C₁₋₆ haloalkylsulfinyl, C₁₋₆ haloalkylsulfonyl, C₁₋₆ haloalkylthio, hydroxyl, nitro and thiol; and

R₅ is H or C₁₋₆ alkyl; or

- a pharmaceutically acceptable salt, solvate or hydrate or a solvate-thereof; provided that:
- a) when R_5 is ethyl, and R_2 , R_3 and R_4 are H then R_1 is not methyl or triphenylmethyl;
 - b) when R_5 is n-pentyl, and R_2 , R_3 and R_4 are H then R_1 is not n-butyl;

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c) when R_5 is methyl, and R_2 , R_3 and R_4 are H then R_1 is not pyrrolidin-1-ylmethyl, 3-tert-butyl-2-hydroxy-5-methyl-benzyl, methyl, or dimethylaminomethyl;

- d) when R_5 is methyl, R_2 is carbomethoxy and R_3 and R_4 are both H then R_1 is not methyl;
- e) when R_2 , R_3 , R_4 and R_5 are all H then R_1 is not 2-amino-2-carboxy-ethyl, pyrrolidin-1-ylmethyl, isopropyl, methyl, benzyl, n-butyl, or carboxymethyl; and
 - f) when R_2 , R_4 , and R_5 are all H and R_3 is methoxy then R_1 is not methyl.
- 2. (currently amended) A compound according to claim 1 wherein:

 R_1 is C_{3-6} cycloalkyl or C_{1-6} haloalkyl, where in each C_{3-6} cycloalkyl or and C_{1-6} haloalkyl group is optionally substituted with 1, 2, 3, or 4 substituents selected form the group consisting of C_{1-6} acyl, C_{1-6} acyloxy, C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarboxamido, C_{2-6} alkynyl, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkylthio, C_{1-6} alkylureyl, amino, C_{1-6} alkylamino, C_{1-6} dialkylamino, carbo C_{1-6} alkoxy, carboxy, cyano, C_{3-6} cycloalkyl, C_{1-6} dialkylcarboxamido, halogen, C_{1-6} haloalkylsulfinyl, C_{1-6} haloalkylsulfinyl, C_{1-6} haloalkylsulfonyl, C_{1-6}

R₂, R₃ and R₄ are each independently selected from the group consisting of H, C₁₋₆ acyl, C₁₋₆ acyloxy, C₂₋₆ alkenyl, C₁₋₆ alkoxy, C₁₋₆ alkyl, C₁₋₆ alkylcarboxamido, C₂₋₆ alkynyl, C₁₋₆ alkylsulfinyl, C₁₋₆ alkylsulfonyl, C₁₋₆ alkylthio, C₁₋₆ alkylureyl, amino, C₁₋₆ alkylamino, C₁₋₆ dialkylamino, carbo C₁₋₆ alkoxy, carboxy, cyano, C₃₋₆ cycloalkyl, C₁₋₆ dialkylcarboxamido, halogen, C₁₋₆ haloalkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkylsulfinyl, C₁₋₆ haloalkylsulfonyl, C₁₋₆ haloalkylthio, hydroxyl, nitro or and thiol; and

R₅ is H or C₁₋₆ alkyl; or a pharmaceutically acceptable salt, solvate or hydrate or a solvate-thereof.

- 3. (currently amended) The compound according to claim 1-or 2 wherein R_5 is C_{1-6} alkyl.
- 4. (currently amended) The compound according to claim 1-or-2 wherein R_5 is H.
- (currently amended) The compound according to any one of claims 1-to 4 wherein R₂,
 R₃ and R₄ are each independently H or halogen.

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(currently amended) The compound according to any one of claims 1-to 4 wherein R₂,
 R₃ and R₄ are each independently H or F.

- 7. (currently amended) The compound according to any one of claims 1 and 3 to 6 wherein R₁ is C₁₋₈ alkyl optionally substituted with substituents selected from the group consisting of C₂₋₆ alkenyl, C₁₋₆ alkoxy, C₂₋₆ alkynyl, C₁₋₆ alkylsulfinyl, C₁₋₆ alkylsulfonyl, C₁₋₆ alkylthio, aryl, substituted aryl, C₃₋₆ cycloalkyl, halogen, C₁₋₆ haloalkoxy, C₁₋₆ haloalkylsulfinyl, C₁₋₆ haloalkylsulfonyl, C₁₋₆ haloalkylthio, heteroaryl, heterocyclyl, and hydroxyl.
- 8. (currently amended) The compound according to any one of claims 1-and 3 to 6 wherein R₁ is selected from the group consisting of 2-butyl, 3-pentyl, 1-propyl, t-butyl, 1-butyl, 4-Methyl-pentyl, 3-methyl-butyl, 1,3-dimethyl-butyl, 3,3-dimethyl-butyl, 1-heptyl, ethyl, 2,2-dimethyl-propyl, and 1-pentyl.
- 9. (currently amended) The compound according to any one of claims 1-and 3 to 6 wherein R₁ is selected from the group consisting of 3-methoxy-benzyl, 4-methoxy-benzyl, 4-methoxy-phenyl ethyl, 3-methoxy-phenyl ethyl, 3,5-difluorobenzyl, and benzhydryl.
- 10. (currently amended) The compound according to any one of claims 1-and 3 to 6 wherein R₁ is selected from the group consisting of 3-isopropoxypropyl, tetrahydro-furan-2-ylmethyl, 2-methoxy-ethyl, 2-ethylsulfanyl-ethyl, 3-hydroxy-propyl, allyl, cyclopropylmethyl, but-2-ynyl, 2-methoxy-1-methyl-ethyl, 2-hydroxy-1-hydroxymethyl-ethyl, 2-ethoxy-ethyl, and 1,2-dimethyl-propyl.
- 11. (currently amended) The compound according to any one of claims 1-to 6 wherein R_1 is selected from the group consisting of cyclopentyl, cyclohexyl, cyclopropyl, and cyclobutyl.
- 12. (currently amended) The compound according to claim 1 selected from the group consisting of:
 - 1-Cyclopentyl-1H-benzotriazole-5-carboxylic acid;
 - 1-(2'-Butyl)-1H-benzotriazole-5-carboxylic acid;
 - 1-(3'-Pentyl)-1H-benzotriazole-5-carboxylic acid;
 - 1-Cyclohexyl-1H-benzotriazole-5-carboxylic acid

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1-Propyl-1H-benzotriazole-5-carboxylic acid;

1-Cyclopropyl-1H-benzotriazole-5-carboxylic acid;

1-(3'-Isopropoxy-propyl)-1H-benzotriazole-5-carboxylic acid;

1-(Tetrahydro-furan-2'-ylmethyl)-1H-benzotriazole-5-carboxylic acid;

1-Cyclobutyl-1H-benzotriazole-5-carboxylic acid;

1-(2-Methoxy-ethyl)-1H-benzotriazole-5-carboxylic acid;

1-(3'Methoxybenzyl)-1H-benzotriazole-5-carboxylic acid;

1-(4'Methoxybenzyl)-1H-benzotriazole-5-carboxylic acid;

1-[2'-(4"-Methoxy-phenyl)-ethylamine]-1H-benzotriazole-5-carboxylic acid;

1-[2'-(3"-Methoxy-phenyl)-ethylamino]-1H-benzotriazole-5-carboxylic acid;

1-(3',5'-Difluorobenzyl)-1H-benzotriazole-5-carboxylic acid;

1-(2-Ethylsulfanyl-ethyl)-1H-benzotriazole-5-carboxylic acid;

1-t-Butyl-1H-benzotriazole-5-carboxylic acid;

1-(3'-Hydroxy-propyl)-1H-benzotriazole-5-carboxylic acid;

1-(1',3'-Dimethyl-butyl)-1H-benzotriazole-5-carboxylic acid;

1-(3',3'-Dimethyl-butyl)-1H-benzotriazole-5-carboxylic acid;

1-Heptyl-1H-benzotriazole-5-carboxylic acid;

1-(2'-Methoxy-1'-methyl-ethyl)-1H-benzotriazole-5-carboxylic acid;

1-(2'-Hydroxy-1'-hydroxymethyl-ethyl)-1H-benzotriazole-5-carboxylic acid;

1-Ethyl-1H-benzotriazole-5-carboxylic acid;

1-Pentyl-1H-benzotriazole-5-carboxylic acid;

1-(2',2'-Dimethyl-propyl)-1H-benzotriazole-5-carboxylic acid;

1-(2'-Ethoxy-ethyl)-1H-benzotriazole-5-carboxylic acid;

1-(1'.2'-Dimethyl-propyl)-1H-benzotriazole-5-carboxylic acid;

1-Benzhydryl-1H-benzotriazole-5-carboxylic acid;

1-Allyl-1H-benzotriazole-5-carboxylic acid;

1-Butyl-1H-benzotriazole-5-carboxylic acid;

1-(Cyclopropylmethyl)-1H-benzotriazole-5-carboxylic acid;

1-(But-2-ynyl)-1H-benzotriazole-5-carboxylic acid;

1-(4'-Methyl-pentyl)-1H-benzotriazole-5-carboxylic acid; and

1-(3'-Methyl-butyl)-1H-benzotriazole-5-carboxylic acid; or

a pharmaceutically acceptable salt, solvate or hydrate thereof.

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13. (currently amended) A pharmaceutical composition comprising a compound according to:

a)-Formula (I):

$$\begin{array}{c|c}
R_2 & O \\
O & O \\
O & R_3
\end{array}$$
(I)

wherein:

 R_1 is H, $G_{1-6}C_{1-8}$ alkyl, C_{3-6} cycloalkyl or C_{1-6} haloalkyl, wherein each C_{1-6} alkyl, C_{3-6} cycloalkyl of and C_{1-6} haloalkyl group is optionally substituted with 1, 2, 3, or 4 substituents selected from the group consisting of C_{1-6} acyl, C_{1-6} acyloxy, C_{2-6} alkenyl, C_{1-6} alkoxy, C_{1-6} alkylcarboxamido, C_{2-6} alkynyl, C_{1-6} alkylsulfinyl, C_{1-6} alkylsulfonyl, C_{1-6} alkylthio, C_{1-6} alkylureyl, amino, C_{1-6} alkylamino, C_{1-6} dialkylamino, carbo C_{1-6} alkoxy, carboxy, cyano, C_{3-6} cycloalkyl, C_{1-6} dialkylcarboxamido, halogen, C_{1-6} haloalkoxy, C_{1-6} haloalkylsulfinyl, C_{1-6} haloalkylsulfinyl,

R₂, R₃ and R₄ are <u>each</u> independently <u>selected from the group consisting of H</u>, C₁₋₆ acyl, C₁₋₆ acyloxy, C₂₋₆ alkenyl, C₁₋₆ alkoxy, C₁₋₆ alkyl, C₁₋₆ alkylcarboxamido, C₂₋₆ alkynyl, C₁₋₆ alkylsulfinyl, C₁₋₆ alkylsulfonyl, C₁₋₆ alkylthio, C₁₋₆ alkylureyl, amino, C₁₋₆ alkylamino, C₁₋₆ dialkylamino, carbo C₁₋₆ alkoxy, carboxy, cyano, C₃₋₆ cycloalkyl, C₁₋₆ dialkylcarboxamido, halogen, C₁₋₆ haloalkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkylsulfinyl, C₁₋₆ haloalkylsulfonyl, C₁₋₆ haloalkylsulfonyl, nitro eff and thiol; and

R₅ is H or C₁₋₆ alkyl; or

a pharmaceutically acceptable salt, solvate or hydrate thereof; or b) any one of claims 1 to 12; wherein said compound is, in combination with a pharmaceutically acceptable carrier.

14. (original) A pharmaceutical composition according to claim 13 further comprising an agent selected from the group consisting of α-glucosidase inhibitor, aldose reductase inhibitor, biguanide, HMG-CoA reductase inhibitor, squalene synthesis inhibitor, fibrate, LDL catabolism enhancer, angiotensin converting enzyme inhibitor, insulin secretion enhancer and thiazolidinedione.

Page 8 of 11 15. (canceled) 16. (canceled) 17. (canceled) 18. (canceled) 19. (canceled) 20. A method of treatment of a metabolic-related disorder comprising (currently amended) administering to an individual in need of such treatment a therapeutically effective amount of a compound-pharmaceutical composition according to claim 13 any one of claims 1 to 12. A method according to claim 20 wherein said metabolic-related disorder is 21. (original) selected from the group consisting of dyslipidemia, atherosclerosis, coronary heart disease, insulin resistance and type 2 diabetes. 22. (canceled) 23. (canceled) 24. (canceled) 25. (canceled) A method of treatment of a metabolic-related disorder comprising 26. (new) administering to an individual in need of such treatment a therapeutically effective amount of a compound according to claim 1.

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27. (new) A method according to claim 26 wherein said metabolic-related disorder is selected from the group consisting of dyslipidemia, atherosclerosis, coronary heart disease, insulin resistance and type 2 diabetes.

28. (new) The pharmaceutical composition according to claim 13 wherein said compound is selected from the group consisting of:

1-Isopropyl-1H-benzotriazole-5-carboxylic acid;

1-Cyclopentyl-1H-benzotriazole-5-carboxylic acid;

1-(2'-Butyl)-1H-benzotriazole-5-carboxylic acid;

1-(3'-Pentyl)-1H-benzotriazole-5-carboxylic acid;

1-Cyclohexyl-1H-benzotriazole-5-carboxylic acid;

1-Benzyl-1H-benzotriazole-5-carboxylic acid;

1-Propyl-1H-benzotriazole-5-carboxylic acid;

1-Cyclopropyl-1H-benzotriazole-5-carboxylic acid;

1-(3'-Isopropoxy-propyl)-1H-benzotriazole-5-carboxylic acid;

1-(Tetrahydro-furan-2'-ylmethyl)-1H-benzotriazole-5-carboxylic acid;

1-Cyclobutyl-1H-benzotriazole-5-carboxylic acid;

1-(2-Methoxy-ethyl)-1H-benzotriazole-5-carboxylic acid;

1-(3'Methoxybenzyl)-1H-benzotriazole-5-carboxylic acid;

1-(4'Methoxybenzyl)-1H-benzotriazole-5-carboxylic acid;

1-[2'-(4''-Methoxy-phenyl)-ethyl]-1H-benzotriazole-5-carboxylic acid;

1-[2'-(3"-Methoxy-phenyl)-ethyl]-1H-benzotriazole-5-carboxylic acid;

1-(3',5'-Difluorobenzyl)-1H-benzotriazole-5-carboxylic acid;

1-(2-Ethylsulfanyl-ethyl)-1H-benzotriazole-5-carboxylic acid;

1-t-Butyl-1H-benzotriazole-5-carboxylic acid;

1-(3'-Hydroxy-propyl)-1H-benzotriazole-5-carboxylic acid;

1-(1',3'-Dimethyl-butyl)-1H-benzotriazole-5-carboxylic acid;

1-(3',3'-Dimethyl-butyl)-1H-benzotriazole-5-carboxylic acid;

1-Heptyl-1H-benzotriazole-5-carboxylic acid;

1-(2'-Methoxy-1'-methyl-ethyl)-1H-benzotriazole-5-carboxylic acid;

1-(2'-Hydroxy-1'-hydroxymethyl-ethyl)-1H-benzotriazole-5-carboxylic acid;

1-Ethyl-1H-benzotriazole-5-carboxylic acid;

1-Pentyl-1H-benzotriazole-5-carboxylic acid;

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1-(2',2'-Dimethyl-propyl)-1H-benzotriazole-5-carboxylic acid;

1-(2'-Ethoxy-ethyl)-1H-benzotriazole-5-carboxylic acid;

1-(1',2'-Dimethyl-propyl)-1H-benzotriazole-5-carboxylic acid;

1-Benzhydryl-1H-benzotriazole-5-carboxylic acid;

1-Allyl-1H-benzotriazole-5-carboxylic acid;

1-Butyl-1H-benzotriazole-5-carboxylic acid;

1-(Cyclopropylmethyl)-1H-benzotriazole-5-carboxylic acid;

1-(But-2-ynyl)-1H-benzotriazole-5-carboxylic acid;

1-(4'-Methyl-pentyl)-1H-benzotriazole-5-carboxylic acid; and

1-(3'-Methyl-butyl)-1H-benzotriazole-5-carboxylic acid; or

a pharmaceutically acceptable salt, solvate or hydrate thereof.